THE

ANTISEPTIC TREATMENT OF PERNICIOUS ANÆMIA.

By G. A. GIBSON, M.D., D.Sc.,

Assistant Physician to the Royal Infirmary, and Lecturer on the Principles and Practice of Medicine at Minto House, Edinburgh.

(*Read before the Medico-Chirurgical Society of Edinburgh, 6th July* 1892; *and reprinted from the Edinburgh Medical Journal for October* 1892.

Being unable to attend the last meeting of the Medico-Chirurgical Society of Edinburgh, it was not in my power to take part, as I had promised, in the discussion on Transfusion in Pernicious Anæmia. The loss was all my own, and it is a matter of great regret to me that I was prevented from hearing the interesting debate which followed Dr Brakenridge's paper. I have endeavoured from the medical press to ascertain the views which were laid before the Society, and I am indebted to the courtesy of the Secretaries for the offer of this opportunity to submit the remarks I had intended to make on the occasion referred to.

My purpose is but a limited one,—to bring before the Society the views of Dr William Hunter, and to state the results which have in my hands followed the adoption of his recommendations.

Briefly stated, the conclusion to which Dr Hunter has been led is that in cases of pernicious anæmia there is excessive hæmolysis. He has arrived at this opinion[1] from observing that in this disease there is a largely increased excretion of urinary pigments, that blood pigment can be detected in cells obviously of renal origin, and that the urine contains a large increase of iron. The symptoms of the disease being so suggestive of something

---

[1] See *The Lancet*, vol. ii. for 1888, pp. 555, 608, and 654; *The Practitioner*, vol. xliii. pp. 161, 321, and 401, 1889; *British Medical Journal*, vol. ii. for 1891, pp. 1 and 81.

R27762

akin to ptomaine poisoning as to lead him to suspect some toxic bodies, analogous to the cadaveric series, to be the cause of the increased blood destruction, he investigated the excretions with the view of ascertaining if they lent any support to this conjecture. From the excretion of aromatic substances he was able to determine that there was no absolute increase in the amount of putrefaction in the alimentary canal, but from the presence of what seemed to be special diamine bodies in the urine he concluded it to be probable that some special organism was the cause of the blood destruction, acting, no doubt, in the alimentary canal.

The practical suggestions which Dr Hunter makes as the result of his elaborate investigations are, that the diet should be as far as practicable fatty and farinaceous, so as to lessen to as great a degree as possible the liability to blood destruction, and that the medicinal treatment should be to combat the tendencies of the disease in the same direction by means of antiseptics,—that which he particularly recommends being β naphthol.

During the latter part of last winter, when, in consequence of the unfortunate illness of Professor Grainger Stewart, his wards were under my care, I had an opportunity of putting Dr Hunter's opinions to the test of experience, and I shall now, without further preface, lay the results before you.

J. C., aged 55, until lately a tea-planter in Northern India, was admitted to Ward XXII. of the Royal Infirmary, 29th January 1892, complaining of weakness and giddiness, with pains in the head and shoulders. The patient had no hereditary tendencies bearing upon the condition then present. While in India he had suffered once from cholera, and he had also had some attacks of malarial fever. Five years ago he suffered from renal calculus on the right side, at which time his urine was, as he says, like claret. The present illness began, about a month before admission, with weakness, giddiness, headache, and palpitation. As these symptoms became progressively worse, he came to Edinburgh for the purpose of placing himself under treatment.

On admission the patient was found to be 5 ft. 6 in. in height; the weight was 11 st. 6 lb. He was well developed and muscular. His complexion was somewhat lemon-tinted, his lips and gums were pale, as were also the conjunctivæ, and he had some œdema about the ankles.

The patient had little appetite, but he had also little thirst. There were no feelings of discomfort during digestion, but there was obstinate constipation. The teeth were good; the tongue was large, pale, flabby, and indented. There was no change in the size of the liver or any of the other abdominal viscera. The fæces were colourless. The pulse was of low tension, moderately filled, regular and equal, its rate being 74 per minute. There was a distinct apex-beat in the fifth interspace, 2¾ in. to the left of the mid-sternal line. At the level of the fourth rib the right edge of the heart was 2¼ in., and the left edge 3¼ in. from mid-sternum. A continuous venous hum was heard over the veins of the neck, and a systolic murmur of very soft character over most of the precordia, with its maximum intensity in the tricuspid area.

On careful examination of the blood with the Thoma-Zeiss hæmacytometer the red corpuscles were found to number 800,000 per cubic millimetre. Changes in size and shape of the red corpuscles were very obvious, but there was no absolute change in the number of the leucocytes. The spleen and lymphatic glands were of normal size. In regard to the respiratory system, there was a history of frequent attacks of epistaxis. There was no change in the fundus oculi. The urine was pale, and no changes of importance were present in it. The temperature was never at any time abnormal.

That this case was one of pernicious anæmia there could be no reasonable doubt, the only characteristic symptoms of that disease which were absent in our patient being retinal hæmorrhages and dark urine.

For the first few days after admission the patient was treated by means of arsenic in various forms, but this had to be discontinued, as the drug produced great gastro-intestinal irritation, showing itself by vomiting and diarrhœa. He was becoming progressively weaker, and the œdema of his feet and legs was increasing; but his blood, frequently examined, remained until 16th February in the same condition, *i.e.*, it contained 800,000 red corpuscles per cubic millimetre.

On 18th February, in addition to the administration of two grains of the protochloride of iron three times a day, the patient was ordered to take small quantities of the perchloride of iron largely diluted with water.

On 2nd March, although the red corpuscles were 920,000 in number, and his weight had reached 11 st. 9 lb., the patient was so reduced in strength that it was clearly necessary to resort to some other means of treatment. The further use of iron was suspended, and it was resolved, with the permission of the patient, which was freely granted, to have recourse to transfusion of blood.

The operation was accordingly performed by Mr Cotterill on the following day,—six ounces of venous blood, carefully defibrinated and diluted with the usual saline solution, being introduced with every precaution into the patient's right arm. There was but little constitutional disturbance in consequence of the transfusion, and on the 4th March the number of red discs had reached 1,120,000. By the 9th March the number had fallen to 1,000,000, and by the 12th March to 920,000. His energy during this time was steadily failing, the œdema was gaining on him, the condition of pulse and heart was becoming worse and worse. The question now before us was whether to have recourse to repeated transfusions or to attempt some other method of treatment. The patient himself was averse to further transfusion, and this fact weighed with us in coming to a decision.

After taking every circumstance of the case into consideration, we resolved to follow the suggestions of Dr Hunter. For two or three days the patient was fed with artificially digested food, and on the 18th March the use of β naphthol was begun, two grains in pill being administered three times a day.

On the 22nd March the number of red discs was 1,000,000, on the 1st April his weight was found to have fallen to 10 st. 10 lb., and on 2nd April the red corpuscles only numbered 800,000. During the three weeks of treatment by means of the β naphthol a good deal of intestinal disturbance had from time to time troubled the patient, and on the 2nd April a severe attack of diarrhœa set in. Whether the drug was the cause or not was uncertain, as at that time there was an epidemic of diarrhœa in the ward; but the attack was severe and lengthy, as in spite of all kinds of medicines the symptom did not abate until a fortnight had nearly passed away. On the 16th April the number of red corpuscles was 1,600,000, and the colour of the skin and mucous membranes was greatly better than at any time since the patient's admission; the œdema, moreover, had quite disappeared, but his weight, as might be expected, was only 10 st. 1 lb.

On the 19th April the administration of the β naphthol was resumed, but the patient only took two pills daily.

On the 23rd April the number of red discs was 1,700,000, and on the 2nd May it had reached 1,850,000. The patient had improved in every way—his strength had greatly returned, his appetite was much better, and his appearance had undergone much improvement. It was considered advisable that he should leave the Infirmary and live in the country, where he might enjoy fresh air; he accordingly took up his abode in the vicinity of Edinburgh on 4th May.

On the 20th May the red corpuscles were 2,000,000, and on the 26th they amounted to 2,080,000. His weight was 10 st. 8 lb., and his strength much greater, so that he was able to take short walks without experiencing much fatigue. He was now permitted to return to his home in Galloway, and was enjoined to continue the use of the β naphthol, to which was added protochloride of iron in doses of two grains twice a day.

On the 18th June the blood was examined by Dr M'Lelland of Wigtown with Gowers' hæmacytometer, and found to contain 1,840,000 red discs. Although there was thus a diminution in the number of the corpuscles, the patient was still improving in strength and energy.

On the 3rd July his weight had risen to 12 st. 1 lb., the number of the red corpuscles was 2,320,000, and the patient was able, without feeling fatigued, to walk more than four miles.

There are many points in this case somewhat difficult of solution.

It will, no doubt, be suggested that the considerable improvement obtained may have been due to the transfusion of blood. This was, however, followed by such a long period unattended by any gain that it seems to me such a suggestion must be dismissed.

One matter of great interest is that during the period of diarrhœa the red corpuscles were doubled. No doubt the drain of fluid from the patient's alimentary tract would not only remove œdema, but would also relatively increase the red corpuscles. It may possibly be held that the doubling of the corpuscles was simply caused in this way, but it is hardly possible that so noteworthy a change in their number could be thus produced; and I am much more inclined to believe that the explanation must be sought in an antiseptic action on the alimentary canal, coincident with the diarrhœa.

What is more difficult to explain is the falling off in the number of the red discs during the first period of administration of the β naphthol, and the later diminution after the patient's return to his home.

It was carefully considered whether there might not be some malarious influence in the case, and the possibility must be granted. No evidence of parasitic causation could be ascertained.

Such are the facts as to this case which I desire to lay before the Society. They are imperfect in many ways, and more especially in not containing any estimation of the hæmoglobin. This omission is due to the epidemic of influenza, which caused so many changes amongst the Resident Physicians as seriously to interfere with the carrying out of continuous observations.

In order to have a control observation as to the effect of antiseptic substances in cases of anæmia which are probably not progressive and pernicious, I have administered β naphthol to a considerable number of patients. So far, there has been in every instance a noteworthy increase in the number of the coloured corpuscles under the influence solely, as far as I am able to judge, of such agents.

One of these cases may be briefly referred to as an example of the effects produced by β naphthol.

K. S., aged 20, unmarried, and employed as a kitchen-maid, came under my observation on 6th May 1892, complaining of breathlessness and headache.

The patient was pale, and her mucous membranes were blanched, but there was no œdema, and the catamenia had undergone no change. On physical examination of the circulatory apparatus, the pulse was found to be of moderate tension; the heart somewhat dilated, the right border extending to 2 inches from the middle line, and the left to 3½ inches in the opposite direction; there was a distinct venous hum in the veins of the neck; and a soft systolic murmur was audible in the tricuspid and pulmonary areas of the precordia. The blood examined by means of the Thoma-Zeiss hæmacytometer, was found to contain 1,950,000 coloured corpuscles per cubic millimetre; some of these were slightly altered in outline, but neither megalocytes nor microcytes were present.

The case appeared to be one of simple anæmia, and was selected in order to ascertain what effect the exhibition of intestinal antiseptics would have upon the state of the blood. The drug administered was β naphthol, two grains of which were given in pill form three times a day after food, and no alteration was made on the food, surroundings, or occupation of the patient.

The number of the coloured corpuscles, as determined from time to time, may be stated in tabular form, as follows:—

6th May 1892	1,950,000
13th „ „	2,450,000
20th „ „	2,675,000
27th „ „	2,550,000
11th June „	2,850,000
2nd July „	3,200,000

In this table is shown a considerable increase, interrupted once by a diminution. This fall in the number of the coloured corpuscles was apparently caused by the occurrence of the catamenial period, which had taken place a few days before the examination of the blood on the 27th May. The general result of treatment by means of an antiseptic substance in the case of an apparently simple anæmia is therefore similar to that observed in regard to pernicious anæmia.

It was not my intention to do more on the present occasion than to lay these facts before the Medico-Chirurgical Society, but it is difficult to abstain from drawing one or two provisional conclusions. The results to some extent support the explanation given by Bunge of the *modus operandi* of iron in the cure of anæmia. I am not sure whether his views have been previously mentioned in the Society or not, and it may be allowed me in a few words to state them. We have the authority of Schmiedeberg for believing that iron, except in organic combination, is not absorbed from the alimentary tract, and, stated succinctly, the explanation advanced by Bunge of the unquestionable effects of iron in almost every form of anæmia is, that such iron as is given medicinally seizes certain unknown poisons formed in the alimentary canal, and prevents them from acting upon the iron contained in the food, and rendering it inert. It seems to me that this theory—which, however, I am informed by my friend Dr Stockman is in some respects not based upon unassailable grounds—receives some support from the results obtained by the use of a substance like β naphthol. And the fact that the continuous use of saline purgatives may in itself, but still better along with iron, remove anæmia—a fact lately urged by Sir Andrew Clark—lends itself to the support of Bunge's view.

In the simple case described above iron would, no doubt, have more quickly cured the patient, but the point I desire to urge is that by antiseptics anæmia may be remedied. In a large number of cases treated by me in hospital work and in private practice, I have found extremely rapid improvement to follow the administration of iron along with β naphthol.

I would finally mention to the Society that in order to obviate the irritation sometimes caused by the β naphthol, I have found the best means of administration to consist in combining it with some bismuth preparation, such as the salicylate.

It is a pleasant duty to express my obligations to Mr Cotterill for his kindness in performing the operation of transfusion in the case of pernicious anæmia which has been narrated, to acknowledge the zealous devotion shown by Drs John Spurway, Stodart Walker, and Cuthbert Thompson in carrying out the details of observation in both cases, and to tender my thanks to Dr M'Lelland for his courtesy in keeping me informed as to the progress of the patient.

Additional Remark.

Since the foregoing observations were laid before the Society, Dr M'Lelland has reported a continued improvement in the condition of his patient. By 3rd August the number of coloured corpuscles had reached 2,830,000 per cubic millimetre, and the weight had risen to 12 st. 5 lb., and on 3rd September they were respectively 3,620,000 and 12 st. 3½ lb.

PRINTED BY OLIVER AND BOYD, EDINBURGH.